## REMARKS

### Rejections under 35 U.S.C.§112, 1st paragraph

Claims 1 and 3-5 have been rejected under 35 U.S.C.§112, 1st paragraph for failing to comply with the written description requirement. More specifically, the Examiner asserts that there was no support in the originally filed specification for deletion of "or during treatment of diseases wherein cyclosporins, FK506 or rapamycin can be exploited." Thus, the Examiner appears to be treating the deletion of the claimed subject matter regarding treatment of diseases in claim 1 as new matter. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The language of claim 1 prior to amendment was in the alternative, i.e. " … tissue transplantation, ***or*** during treatment diseases wherein cyclosporins, FK506 or rapamycin can be exploited". Thus, it is clear from the original claim language and specification that Applicants contemplated two different embodiments of the invention, one of avoiding undesirable side effects during organ and tissue transplantation and one of avoiding undesirable side effects during treatment. There is no procedural or legal requirement that all contemplated embodiments must be recited in the claims, instead of just one of the embodiments. As such, deletion of one embodiment

of the invention from the claims is not new matter and withdrawal of the rejection is respectfully requested.

The Examiner maintains the previous rejection of Claim 1 under 35 U.S.C.§112, 1st paragraph for failing to be described in the specification in such a way so as to convey to one skilled in the art that the inventors were in possession of the invention at the time the application was filed. In response to Applicants' arguments of July 23, 2003, the Examiner asserted that the arguments were insufficient to overcome the rejection because "the claimed invention is not limited to art known peptides" and that claim 1 "encompasses any peptide with the particular functional attributes recited in the claim". Applicants traverse this rejection and withdrawal thereof is respectfully requested.

In the reply of July 23, 2003, Applicants argued that the high-affinity binding sites of the interferons have been characterized and are well-known (See the *FEBS Lett.* and *Mol. Immunol.* articles by Zav'yalov V.P. *et al.*). Thus, Applicants are not merely relying on functional characteristics to define the present invention (pertaining to the Examiner's comments that the present invention "encompasses any peptide with the particular functional attributes recited in the claim"). Instead, Applicants have referred the

Examiner to other structural features demonstrating that one skilled in the art would understand that the present inventors had possession of the claimed invention (at the time of filing the application).

However, in the interest of facilitating the allowance of the application, Applicants have incorporated the subject matter of claim 3 into claim 1. Withdrawal of the rejection is therefore respectfully requested.

**Rejections under 35 U.S.C. §102(b)**

Claims 1, 3 and 19 have been newly rejected under 35 U.S.C.§102 as being anticipated by Gryn et al. Gryn et al. is asserted to teach a composition of cyclosporin and interferon α in a composition having the agents in separate containers. The Examiner further asserts that the functional properties recited in the claims are inherent properties of composition of Gryn et al. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The invention of claim 1 is drawn to a composition having immunosuppressants, cyclosporins, FK506, or rapamycin and at least one bioactive peptide comprising the high-affinity binding/anti-lymphoproliferative site of interferons α, β, ω, τ, or recombinant

proteins carrying one or more of the sequences, wherein said bioactive peptide comprises one or more of the sequences of SEQ ID NO: 1 or a variant thereof that is SEQ ID NO: 2, such that at up to three amino acids of SEQ ID NO: 1 are substituted, for the aim of amplification of immunosuppressants' activities to decrease their therapeutic dose, and as the consequence to avoid their undesirable side effects during organ and tissue transplantation.

The Examiner appears to rely on the disclosure of cyclosporin and interferon α at page 22, second column of Gryn *et al.* (*Bone Marrow Trans.*, Vol. 19, pages 221-226 (1997)), which are administered separately, to account for the features of claims 1, 3 and 19.

Gyrn et al. disclose the use of cyclosporin A and natural interferons (interferon α) in a combination treatment of non-Hodgkin's lymphoma. The present invention has been limited to compositions, which comprise specific peptides of SEQ ID NOS: 1 and/or 2. Since the present invention does not use naturally occurring interferon, but peptide fragments, the composition of Gryn et al. is different from and does not anticipate the present invention. The specification on page 5, lines 18-20 discusses the advantages to using small peptides in the present invention.

In addition, Applicants disagree with the Examiner's interpretation of Gryn et al. as teaching a "composition." Gryn et al. does not disclose a composition but rather the administration of a loading dose of cyclosporin at day 1 of bone marrow transplantation, followed by a lower dose continuing to day 28. As soon as the platelet count was satisfactory (at a median time of 24 days post transplant, See Abstract), the patients began treatment with α-inteferon, administration of which continued for 2 years. Thus, there may be some small overlap in time wherein the patients are being given both drugs. However even in the instances of drug overlap with Gryn et al., the two drugs are always administered separately, never as a composition.

The Examiner has mischaracterized the present invention as encompassing a composition wherein the components are separate. The Examiner's reliance on claim 5 of the Finnish priority document is misplaced. As a first point, even if claim 5 of the Finnish priority document recites having the two drugs in separate containers, the present invention is not so claimed in the instant claims. The Examiner has ignored the plain meaning of the pending claims, i.e. that the composition has immunosuppressants, cyclosporins, FK506, or rapamycin **and** at least one bioactive peptide.

In addition, even with the disclosure in the FI '121 application of having the two drugs in separate containers, the drugs are still administered at the same time, i.e. the drugs are administered simultaneously during transplantation. This is completely different from Gryn et al. wherein cyclosporin and interferon α are taught as two separate compositions, one administered during transplantation and one administered subsequent to transplantation. Thus, Gryn et al. does not disclose a composition containing immunosuppressants, cyclosporins, FK506, or rapamycin **and** at least one bioactive peptide and Gryn et al. fails to anticipate the present invention.

Claim 1 has been rejected under 35 U.S.C.§102 as being anticipated by Yoshida et al. Claim 1 has been amended to incorporate the subject matter of claim 3. As such, this rejection is rendered moot and withdrawal thereof is respectfully requested. In addition, as discussed above, the Examiner has mischaracterized the present invention as encompassing a composition wherein the components are separate. The Examiner's reliance on claim 5 of the Finnish priority document is misplaced. The Examiner has ignored the plain meaning of the pending claims, i.e. that the composition has immunosuppressants, cyclosporins, FK506, or rapamycin **and** at

least one bioactive peptide. Withdrawal of the rejection is therefore respectfully requested.

**Rejections under 35 U.S.C.§103**

Claims 1, 3, 5 and 19 have been rejected under 35 U.S.C.§103 as being obvious over Gryn et al. combined with Zav'Yalov et al. and Fish. As discussed above, Gryn et al. is asserted to teach a composition of the invention. Gryn et al. is said to differ from the invention in failing to teach peptides of SEQ ID NO:1 or 2. Zav'Yalov et al. is relied upon for teaching a bioactive peptide of amino acids 130-137 of interferon α2, which interacts with the high affinity site of interferon α2. The peptide of Zav'Yalov et al. is asserted to meet the recited features of SEQ ID NO:1. Fish is similarly asserted to teach interferon α2 peptides that meet the features of SEQ ID NO:2. The Examiner asserts that it would been obvious to use the peptides of Zav'Yalov et al. and Fish in the "composition" of Gryn et al. and thus achieve the invention. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The rejection is based on the erroneous premise the Gyrn et al. teaches a "composition" having immunosuppressants, cyclosporins, FK506, or rapamycin **and** at least one bioactive peptide. As

discussed above, Gryn et al. teach the separate administration of one drug during transplantation and of the second drug subsequent to transplantation. Gryn et al. fails to disclose a "composition" of both drugs as recited in claim 1. Nor is there any suggestion of a composition of the instant invention from Gryn et al. because an essential feature to Gryn et al. is that the drugs are administered at separate stages of transplantation, i.e. with the first drug being giving during transplantation for a relatively short time of 28 days and the second drug being given following transplantation for a prolonged period measured in years. As such, it is not possible to achieve the invention even if the peptides of Zav'Yalov et al. or Fish are used in replace of the natural interferon of Gryn et al. Withdrawal of the rejection is therefore respectfully requested.

Claim 4 has been rejected under 35 U.S.C.§103 as being obvious over Gryn et al. combined with Zav'Yalov et al., Fish and Isoai et al. Further to the asserted teachings of Gryn et al., Zav'Yalov et al. and Fish, Isoai et al. is asserted to teach a peptide chemically coupled to albumin to form stable entities. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

As discussed above, the Gryn et al. fails to teach a composition of the instant invention. As such, for the reasons

discussed above, the secondary references, including Isoai et al. fail to compensate for the deficiencies of Gryn et al. and fail to teach or suggest the present invention. Withdrawal of the rejection is therefore respectfully requested.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petition for a three (3) months extension of time for filing a reply in connection with the present application, and the required fee of $55.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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